fibrosis. These include high incidence of nasal polyps, severe intractable pulmonary disease with wheezing, and serum and sputum factors which inhibit ciliary action. Further identification of this inhibitor may shed light on the pathogenesis of both diseases.

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REFERENCES

Kulczycki LL, Mueller H, Schwachman H: Respiratory allergy in patients with cystic fibrosis. JAMA 175:358, 1961

Day G, Mearns M: Bronchial liability in cystic fibrosis. Arch Dis Child 48:355, 1973

Caplin I, Haynes JT: Possible genetic links between cystic fibrosis of the pancreas and aspirin sensitive asthma. Ann Allergy 31:320, 1973

## Genetics in Atopy

THE HEREDITARY NATURE of atopic allergic states, such as hayfever, asthma and eczema, has been known for half a century. Vaz and Levine discovered that gamma E immunoglobulin (IgE) antibody production in inbred strains of mice was under two sets of genetic controls. One causes elevated serum IgE antibodies to many antigens and the second controls reagin-production response to only certain antigens. The latter, termed an Ir (immune response) gene was linked closely to the H-2 major histocompatibility locus in mice. Such Ir genes described earlier by McDevitt and Benacerraf responded to synthetic polypeptides or minute doses of protein antigens.

Levine et al noted that the protein antigen dosage of pollens that one person inhales during a whole pollen season is extremely small, for example, 1 $\mu$g of ragweed antigen E (AgE) during a three-month ragweed season in New York. They wondered if there was an immune response gene in certain persons which could respond with IgE production to ragweed AgE. In seven families with a propositus and several other members with ragweed hayfever, they found that persons with clinical hayfever and intense wheal and flare skin tests to ragweed AgE all had the same HL-A histocompatibility haplotype which they called the "hayfever haplotype." There was, however, no single common "hayfever haplotype" in the seven families. Of 26 members of the seven families with the "hayfever haplotype," 20 had clinical hayfever and positive ragweed AgE skin tests. None of 11 family members who had the other haplotype of the propositus (and lacked the "hayfever haplotype") had clinical hayfever. These results were highly significant statistically ($p<.01$). Furthermore, none of 20 family members with neither haplotype of the propositus had hayfever. The close association between HL-A haplotype, clinical hayfever, and IgE antibody production in successive generations in man resembled the immune response gene associated with H-2 histocompatibility loci in mice. These findings suggest that tissue typing of infants born into allergic families might identify those at risk from allergic disease.

Marsh et al surveyed a population of 105 unrelated ragweed sensitive patients with positive findings for ragweed AgE from skin and leukocyte histamine release tests. Seventeen of these patients were highly sensitive to a minor antigenic determinant of ragweed called Ra5 (molecular weight 4,700), 77 percent were Ra5-insensitive and ten had intermediate sensitivity. HL-A typing of this population showed a highly significant correlation between HL-A7 and closely related group tissue types and high sensitivity to Ra5 ($p<0.003$) relative to frequency of those tissue types in the Ra5-insensitive group. This suggested to them that a certain immune response gene located at or near an HL-A locus controlled the immune responsiveness of a person to ragweed Ra5.

Hamburger and Bazaral at the University of California, San Diego, reported that total serum IgE levels in 26 pairs of monozygotic twins were very close, while IgE levels in dizygotic twins varied as greatly as in the general population. They suggested that serum IgE level is controlled genetically, as in Levine and Vaz's first group of mice.

Intensive efforts are underway in many laboratories for a better understanding of the familial occurrence of allergy on the basis of immune response genes.

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REFERENCES

Levine BB, Stember RH, Fotino M: Ragweed hay fever: Genetic control and linkage to HL-A haplotypes. Science 178: 1201-1203, Dec 15, 1972

Marsh DG, Bias WB, Hsu SH, et al: Association of the HL-A7 cross-reacting group with a specific reaginic antibody response in allergic man. Science 179:691-693, Feb 16, 1973

Hamburger RN, Bazaral M: Standardization and stability of immunoglobin E (IgE). J Allergy Clin Immunol 49:189-191, Mar 1972

Cooke RA, VanderVeer A: Human sensitization. J Immunol 1:201, 1916

Vaz NM, Levine BB: Immune responses of inbred mice to repeated low doses of antigen: Relationship to histocompatibility (H2 type). Science 168:852, 1970

Vaz NM, Levine BB: Effect of combinations on inbred strain antigen and antigen dose on immune responsiveness and reagin production in the mouse (A potential mouse model for immune aspects of human atopic allergy). Int Arch Allergy 39:156, 1970

McDevitt HO, Benacerraf B: Immune response genes. Adv Immunol 11:31, 1969